REMARKS

1. The Examiner alleges that claims 36, 39, 42, 45 and 48 are confusing in that they depend from claim 26, which claim was not elected for prosecution.

The elected claims 36, 39, 42, 45 and 48 have now been amended to recite the boron-containing hapten of formula I. Claims 36, 39, 42, 45 and 48 describe a catalytic antibody that catalyzes a chemical reaction of interest and method of producing such antibody. The boron-containing hapten that elicits the catalytic antibody is described by formula I. Therefore, claims 36, 39, 42, 45 and 48 constitute the same invention.

2. The Examiner rejects claims 36, 39, 42, 45 and 48 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctively claim the subject matter which applicant regards as the invention.

This objection has been remedied by incorporating the hapten of formula I into the elected claims.

3. The Examiner objects to claim 42 as not being consistent with claim 39.

Claim 42 has been amended to be consistent with claim 39.

4. The Examiner objected to instructions in the preliminary amendment (4/3/99), reciting the first two applications in the lineage (08/333, 237 and 07/190, 271) in the first paragraph of the specification while the next two applications of the lineage are recited in the second paragraph. These two recitations need to be included together in the first paragraph of the specification.

This has been remedied.

5. The Examiner rejects claims 36, 39, 42, 45 and 48 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully submit that the presently claimed subject matter is fully enabled. The first paragraph of 35 U.S.C. §112 requires nothing more than objective enablement. Whether this is achieved by illustrative examples or by broad terminology is of no importance. *In re Marzocchi*, 169 U.S. P.Q. 367 (CCPA 1971). An assertion by the Patent Office that the enabling disclosure is not commensurate with the scope of the protection sought must be supported by evidence or reasoning substantiating the doubt so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (CCPA 1974); *In re Bowen*, 181 U.S.P.Q. 48 (CCPA 1974); *In re Armbruster*, 185 U.S.P.Q. 152 (CCPA 1975).

With respect to the Examiner's assertion that the "specification teaches how to make the hapten but does not teach that this hapten can be used to make catalytic antibodies or that these catalytic antibodies can be used to cleave the bonds listed in the claims", the specification teaches how the hapten can be used to make catalytic antibodies and how these catalytic antibodies can be used to cleave the bonds listed in the claims. Contrary to the suggestion in the Office Action, actual examples are not required to comply with the first paragraph of 35 USC 112; *Shanks v. Scheffer*, 204 U.S.P.Q. 781, 783; *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q. 2d 1302, 1304 (Fed. Cir. 1987); See MPEP 2164.02.

Applicants urge that is improper to reject claims on the ground that the specification does not support the claims when the terms of the claims are no broader than the broadest description of the invention in the specification and there is not reason to challenge the operativeness of the subject matter embraced by the claims. *Ex parte Altermatt*, 183 U.S.P.Q. 436 (Bd. Pat. App. Int. 1974).

To assert a rejection for lack of enablement, the Examiner must meet the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). See also, MPEP §2164.04. The Examiner has failed to present any evidence or reasoning substantiating the allegation that the presently claimed subject matter is not enabled. Accordingly, the burden of proving enablement has not shifted to the Applicants and therefore the rejection is improper.

Applicants further note that the test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re angstadt*, 190 U.S.P.Q. 214 (CCPA 1976). See also, MPEP §2164.01. The fact that experimentation may be complex does not necessarily make it undue if those skilled in the art typically engage in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983); *M.I.T. v. A.B. Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985); *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). See also, MPEP §2164.01.

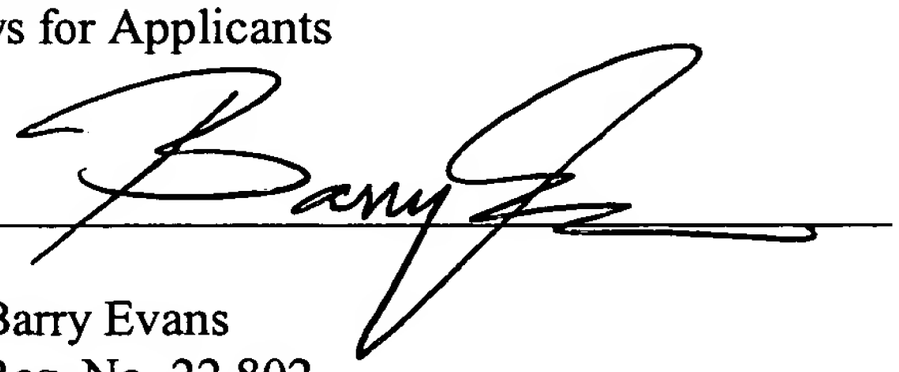
Even assuming arguendo that a reasonable basis for objecting to the specification was set forth in the Office Action, the description provided in the specification is sufficient to overcome the objection. Moreover, for the Examiner's convenience, Applicants enclose an article entitled "Direct Selection for Catalysis from Combinatorial Antibody Libraries Using a Boronic Acid Probe: Primary Amide Bond Hydrolysis", *Journal of the American Chemical Society*, Volume 120, Number 10 (March 18, 1998) which demonstrates that similar trigonal boron containing haptens are well suited to be employed as transition state analogs for making catalytic antibodies that cleave amide bonds (see, "conclusions" on page 2217). Thus, there is not reasonable basis to assert that the presently claimed subject matter is not enabled.

6. The Examiner objected to the priority data being inserted into two different paragraphs in the specification.

The priority data has been combined into one paragraph as suggested by the Examiner.

Respectfully submitted,

KRAMER LEVIN NAFTALIS & FRANKEL LLP
Attorneys for Applicants

By: 

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PATENT
[100390-2140]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Powell et al.
Serial No.	:	09/303,716
Filed	:	April 30, 1999
For		**TRANSITION STATE ANALOGS**
Group Art Unit	:	1652
Examiner	:	Charles L. Patterson, Jr.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Assistant Commissioner for Patents,
Washington, D.C. 20231, on April 17, 2001

Barry Evans, Reg. No. 22,802
Name of Applicant, Assignee or Registered Representative

Signature

April 17, 2001
Date of Signature

AMENDMENT

(Marked-Up Version)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Official Action mailed October 17, 2000, a marked-up version of the specification and claims of the above identified patent application is as follows:

IN THE SPECIFICATION:

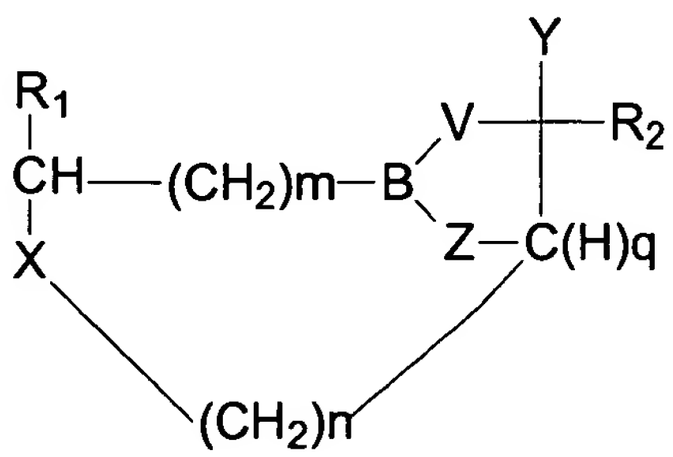
Under Field Of The Invention, delete second paragraph on page 2 and substitute the following paragraph:

This application is a continuation of Application Ser. No. 08/333,237, filed November 2, 1994, which is a continuation of Application Ser. No. 07/190,271, filed June 4, 1988, now abandoned, which was a continuation-in-part of Application Ser. No. 674,253, filed November 27, 1984, which [is] was a continuation-in-part of application Ser. No. 556,016, filed November 29, 1983, now abandoned, the contents of which applications are hereby incorporated by reference into this application.

The changes in this paragraph includes no new matter.

IN THE CLAIMS:

36. (Amended) A catalytic antibody elicited by an antigen comprising the boron-containing hapten of [claim 26] formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said

hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, $(C_2–C_4)$ alkyl, $–CH_2CH(CO_2H)_2$, $–(CH_2)_2 S(O)CH_3$, $–(CH_2)_2 S(O)_2 CH_3$, $–(CH_2)_3 NH_2$ or $–(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, $(C_1–C_9)$alkyl, $(C_1–C_9)$ alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkoxy or $(C_1.C_4)$alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, $(C_1–C_9)$alkyl, $(C_1–C_9)$alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, $(C_1–C_4)$alkyl, $(C_1$-$C_4)$alkoxy or $(C_1.C_4)$alkoxycarbonyl; and wherein

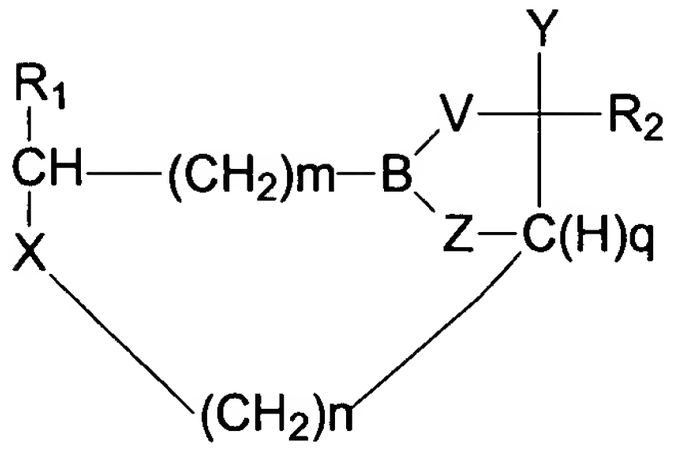
Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

39. (Twice Amended) A catalytic antibody which catalyzes a chemical reaction of interest and which is elicited through *in vitro* or *in vivo* techniques by an antigen comprising the boron-containing hapten of [claim 26] formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, $-CH_2CH(CO_2H)_2$, $-(CH_2)_2 S(O)CH_3$, $-(CH_2)_2 S(O)_2 CH_3$, $-(CH_2)_3 NH_2$ or $-(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein

the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

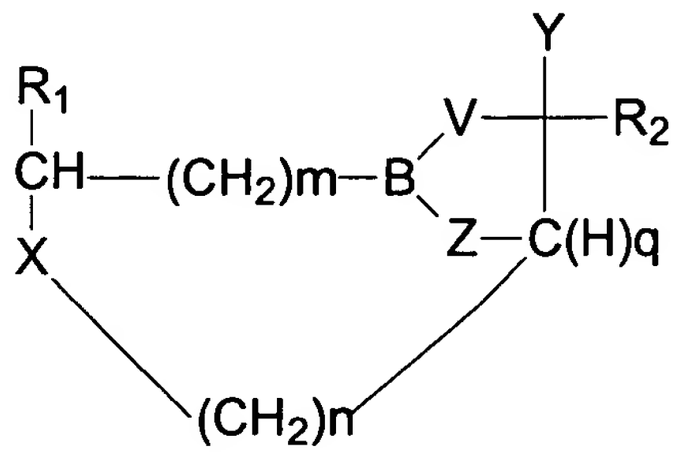
said catalytic antibody having been prepared by a process comprising the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

42. (Twice Amended) A method for producing catalytic antibodies which catalyzes a chemical reaction of interest and which are elicited through *in vitro* [in vitro] or *in vivo* [in vivo] techniques by an antigen comprising the boron-containing hapten of [claim 26] formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, $-CH_2CH(CO_2H)_2$, $-(CH_2)_2 S(O)CH_3$, $-(CH_2)_2 S(O)_2 CH_3$, $-(CH_2)_3 NH_2$ or $-(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

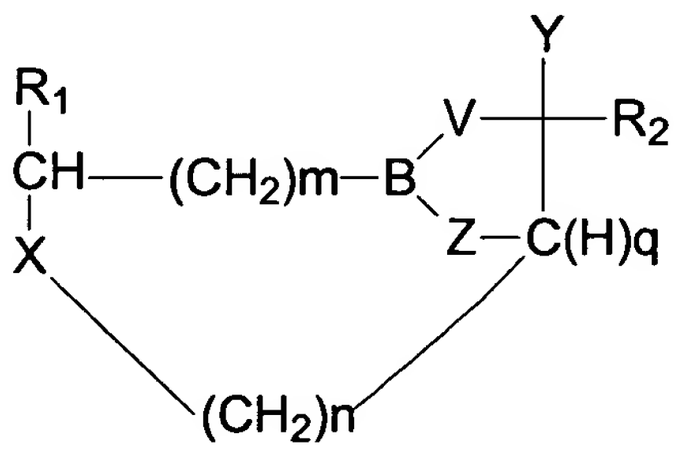
wherein said method comprises the steps of:

(a) exposing cells capable of producing antibodies to said antigen and thereby generating antibody producing cells;

(b) hybridizing said antibody producing cells with myeloma cells and thereby generating a plurality of hybridoma cells each producing monoclonal antibodies; and

(c) screening said plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes said chemical reaction of interest.

45. (Amended) A method for catalyzing the cleavage or formation of a peptide linkage or an ester bond in a molecule comprising contacting said molecule with an effective amount of a catalytic antibody elicited by an antigen comprising the boron-containing hapten of [claim 26] formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, $(C_2–C_4)$ alkyl, $–CH_2CH(CO_2H)_2$, $–(CH_2)_2 S(O)CH_3$, $–(CH_2)_2 S(O)_2 CH_3$, $–(CH_2)_3 NH_2$ or $–(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

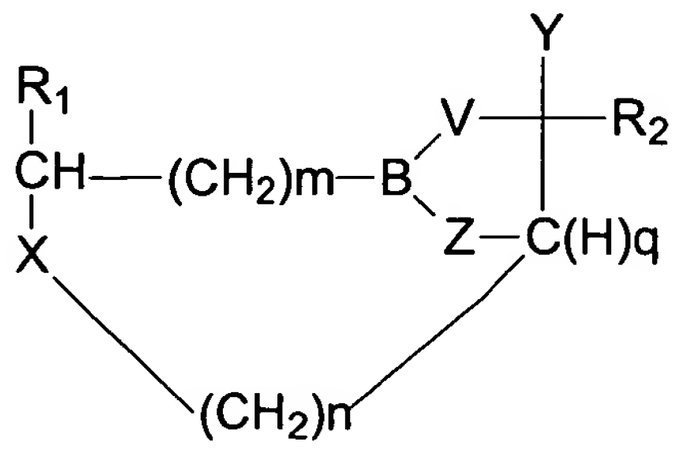
Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z.

48. (Twice Amended) A method for catalyzing the cleavage or formation of a specific peptide linkage or an ester bond within a specific amino acid sequence of a molecule which comprises: contacting said molecule with an effective amount of a catalytic antibody elicited with a boron-containing hapten of [claim 26] formula I,



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wherein

R_1 and R_2 may be the same or different and each is a side chain of a naturally occurring amino acid, a hydroxy containing side chain of a naturally occurring amino acid wherein said hydroxy group may be glycosylated, phosphorylated, sulphonylated or protected by a hydroxy protecting group, a primary amido containing side chain of a naturally occurring amino acid wherein said amido group may be glycosylated, (C_2–C_4) alkyl, $-CH_2CH(CO_2H)_2$, $-(CH_2)_2 S(O)CH_3$, $-(CH_2)_2 S(O)_2 CH_3$, $-(CH_2)_3 NH_2$ or $-(CH_2)_3 ONHC(=NH)NH_2$;

V is O, CH_2 or NH;

X is hydrogen, oxygen, amino, amino protected by a terminal amino protecting group, amino bonded to the C terminus of a naturally occurring amino acid to form a peptide bond, amino bonded to the C terminus of a peptide to form a peptide bond, alkene, (C_1–C_9)alkyl, (C_1–C_9) alkoxy or phenyl, phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl, wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkoxy or (C_1-C_4)alkoxycarbonyl;

Y is hydrogen, carboxyl, carboxyl protected by a terminal carboxyl protecting group, a carbonyl bonded to the N terminus of a peptide through a peptide bond, (C_1–C_9)alkyl, (C_1–C_9)alkoxy, phenyl phenoxy, cyclohexyl, phenylthio, phenylsulfinyl or phenylsulfonyl wherein the aforementioned phenyl groups may be unsubstituted or mono-, di- or trisubstituted by halogen, (C_1–C_4)alkyl, (C_1-C_4)alkoxy or (C_1-C_4)alkoxycarbonyl; and wherein

Z is O, CH_2 or NH;

m is 0 or an integer from 1 to 10;

n is 0 or 1; and

q is 1 or 2 provided that if q is 2, then n=0 and there is no bond between X and the carbon bound to Z,

said hapten being [to] homologous to said specific amino acid sequence.

Respectfully submitted,

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